JACC Vol. 29, No. 3
March 1, 1997:519–25

Correlation of Angiographic Morphology and Clinical Presentation in Unstable Angina

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Objectives. **This study sought to correlate angiographically detected complex lesions and intracoronary thrombus with the severity of clinical presentation in unstable angina (UA).**

Background. **Unstable angina is usually related to acute thrombosis superimposed on a disrupted plaque. Complex and thrombotic lesions are more prevalent in UA and have been associated with a worse prognosis. The highest levels of the Braunwald classification of UA (III = rest angina within 48 h of presentation; C = postinfarction angina; and c = angina refractory to maximal medical therapy) can be used to assess the severity of clinical presentation, but they have not been directly correlated with thrombotic and complex lesions.**

Methods. **We conducted a prospective study of 284 patients with UA who underwent cardiac catheterization. A single angiographer with no knowledge of the clinical classifications interpreted all angiograms. Culprit lesions identified in 200 patients were classified as simple or complex. Complex lesions included the categories complex morphology, intracoronary thrombus (ICT) or total occlusion. Lesions were also quantitatively analyzed, and Thrombolysis in Myocardial Infarction (TIMI) flow was assessed. Univariate and multivariate logistic regression analyses of the angiographic findings were performed controlling for all cardiac risk factors, previous angioplasty or bypass surgery and multivessel disease, and we sequentially compared Braunwald classes III, C and c with classes <III, <C and <c, respectively.**

Results. **Class III was associated with complex lesions ($p = 0.04$) and decreased TIMI flow ($p = 0.03$). Class C angina correlated with complex lesions ($p = 0.04$), ICT ($p = 0.005$) and decreased TIMI flow ($p = 0.03$). Class c angina was associated with ICT ($p = 0.02$). The degree of stenosis by quantitative angiography was not associated with any particular Braunwald class.**

Conclusions. **Recent rest pain and refractory or postinfarction UA, or both, are strongly associated with the general category of complex lesions and specifically with angiographically detected ICT and decreased TIMI flow.**

(J Am Coll Cardiol 1997;29:519–25)

The pathogenesis of unstable angina (UA) represents one side of the spectrum of the acute coronary syndromes (1). These syndromes share, in the majority of cases, the common mechanism of coronary occlusion due to acute thrombus formation superimposed on a disrupted or fissured atherosclerotic plaque (2). A higher incidence of angiographically detected thrombus has been documented as we shift from UA to non-Q and Q wave myocardial infarction (MI) (3–5).

Unstable angina as a clinical diagnosis incorporates a diverse group of clinical presentations that occupy an intermediate position between the more strictly defined clinical entities of acute MI and chronic stable angina. Accelerated angina and rest angina are both considered unstable, but accelerated angina without rest pain appears to be a more benign condition than rest angina (6). Therefore, clinical heterogeneity within this syndrome may represent different degrees of severity of the same mechanism or existence of other mechanisms, or both. Although complex coronary lesions or intracoronary thrombus (ICT), or both, have been angiographically defined in different ways by various investigators, their presence has been uniformly associated with UA and MI as opposed to stable angina (7–10). It is conceivable that a gradual increase in angiographic thrombotic features exists within the diverse UA patient population. However, establishment of such a precise relation to the heterogeneous clinical presentations of patients with UA has not yet been achieved.

Although new markers of myocardial injury and necrosis have been developed and are currently evaluated in clinical studies (11–13), a definitive laboratory or electrocardiographic (ECG) finding that confirms the diagnosis and determines the severity of UA has not yet been identified. One of these new markers, troponin T, has been preliminarily reported to be associated with coronary morphology in a small study (13). The Braunwald classification was introduced in 1989 to subdivide the patients with UA according to clinical characteristics and to provide better prognostic stratification (14). The complexity of the classification reflects the extent of the clinical diversity of

From the Cardiovascular Institute, Mount Sinai Medical Center, New York, New York. This study was presented in part at the 45th Annual Scientific Session of the American College of Cardiology, Orlando, Florida, March 1996.

Manuscript received July 3, 1996; revised manuscript received November 21, 1996, accepted November 26, 1996.

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0735-1097/97/$17.00
PII S0735-1097(96)00560-8

Abbreviations and Acronyms

ECG = electrocardiographic
ICT = intracoronary thrombus
MI = myocardial infarction
QCA = quantitative coronary angiography
TIMI = Thrombolysis in Myocardial Infarction
UA = unstable angina

patients with UA and the many variables that need to be accounted for to appropriately stratify patients. The validity of the particular classification system to predict patient outcome has been only recently investigated systematically (15,16). A combined angiographic score indicative of lesion complexity was shown in a retrospective study (17) to correlate with a combination of higher Braunwald classes. In the present study, we directly correlated angiographic findings of intracoronary thrombus and complex lesions with the patients' level of symptoms, using each of the higher Braunwald classes as a measure of the acuteness or severity, or both, of the clinical presentation of UA.

Methods

Patients. We conducted a prospective study of 284 patients who were referred to our cardiac catheterization laboratory for diagnostic angiography with the clinical diagnosis of UA during a period of 6 months. During this time, ~450 patients were admitted to the hospital with a clinical diagnosis of UA, and 400 of them were referred for angiography. All study patients were interviewed on the day of angiography, and their charts were reviewed to confirm the referring diagnosis and to identify the localization of the ECG changes during chest pain episodes. Assignment of a UA class according to the Braunwald classification was done on the day of the procedure by one of two investigators (G.D., R.H.) before angiography. Patients without significant coronary disease (<70% diameter stenosis) or with elevated creatine kinase levels (more than twice normal values) and creatine kinase-MB fraction indicative of acute MI were excluded, as were patients with restenosis of the culprit lesion after previous coronary intervention.

Braunwald classification. Patients with a noncoronary disease cause identified as responsible for the unstable clinical syndrome were classified as Braunwald class A (secondary UA), patients with primary UA as class B and patients with UA within 14 days of a myocardial infarction as class C (14). New onset exertional chest pain and accelerated angina without rest pain were classified as class I, rest angina without pain for 48 h before angiography as class II and recent (<48 h) rest angina as class III. The intensity of medical therapy was reflected in classes a, b and c. Patients with UA and no or minimal therapy (i.e., only aspirin and one class of antianginal agents) formed class a; patients with angina refractory to maximal medical therapy, including intravenous nitroglycerin and heparin, formed class c; and class b was formed by the remaining patients. The original classification did not include use of antithrombotic agents in the latter category. However, aspirin and heparin are currently considered standard therapy for UA and thus were included within the criteria for "maximal" medical therapy. Classes III, C and c were individually considered indicators of the most acute or severe, or both, clinical presentations. Although the presence or absence of ECG changes had also been proposed by Braunwald as another criterion for UA severity, we used ECG changes with chest pain solely to localize the ischemia-related (culprit) lesion.

Cardiac catheterization. All patients underwent diagnostic coronary angiography with the transfemoral approach using the Judkins technique. The procedure was performed within 48 h of presentation to the hospital, as per the standard routine of the catheterization laboratory. All obstructive lesions were visualized in two orthogonal views. Qualitative morphologic analysis of all angiograms was performed by a single experienced angiographer (J.A.A.) who had no knowledge of the patients' Braunwald classification. In each case we attempted to identify the ischemia-related artery and a single culprit lesion with a visual diameter stenosis ≥70% on the basis of coronary anatomy alone or localization of ECG changes with pain, or both. Intraarterial flow was graded (grades 0 to 3) according to the Thrombolysis in Myocardial Infarction classification (TIMI) (18).

Culprit lesion determination. In patients with single-vessel disease, the ischemia-related (culprit) artery was considered to be the diseased vessel. In patients with multivessel disease, the culprit vessel was identified by coronary anatomy or localization of ECG changes with pain, or both. In case there was more than one obstructive lesion in the ischemia-related vessel, the culprit lesion was considered to be the most severe narrowing or the lesion with complex morphology or ICT, or both. If there were no ECG changes, the culprit lesion was considered to be the complex lesion or the lesion with angiographic thrombus, or both. All culprit lesions had to have at least 70% visual diameter stenosis. In the absence of such a lesion, or in the presence of more than one such lesion, the patient was excluded from subsequent analyses because a single culprit lesion was not identified.

Coronary morphology. All cine films were reviewed on a Vanguard XR-35 and magnified fourfold for analysis of coronary morphology. Culprit lesions were qualitatively classified as either simple or complex. The term *complex lesion* included three angiographic definitions, all of which were thought to indicate the presence of thrombus. A complex lesion included the presence of a stenosis that was usually but not always eccentric, with either ulcerations, irregular borders or overhanging edges, according to the criteria for complex morphology as proposed by Ambrose et al. (7). The definition of a complex lesion also included any culprit lesion with intracoronary filling defects or total occlusion. *Intracoronary thrombus* was defined as a filling defect proximal or distal to the culprit lesion, visible in multiple projections, with at least three edges surrounded by contrast agent (19). Total occlusions and ICT

were considered complex lesions, but were also classified as separate angiographic variables in our analysis for comparison with other studies of angiographic morphology in UA. By these definitions we considered that complex lesions without ICT (*filling defects*) contained some amount of thrombus, either *quantitatively* (smaller vs. larger amount) or *qualitatively* (platelet vs. fibrin thrombus) different from angiographically detected ICT. *Simple lesions* were defined as stenoses with smooth borders without evidence of any complex features, as previously described.

Quantitative coronary angiography (QCA) of the culprit lesion was performed in patients with patent arteries by a single operator (N.A.C.) who had no knowledge of the patients' Braunwald classification and qualitative coronary morphology. The QCA analysis was done in two orthogonal views that best showed the lesion without overlap or forshortening, using videodensitometric measurements of the lesion and the "normal" vessel (Vanguard Analyzer XR-70) (20). The final QCA result was considered the average of the two views.

Statistical analysis. The independent association of the Braunwald classes III, C and c with the presence of ICT or a complex lesion, or both, were the primary end points of the study. Secondary end points were the association of total occlusions and decreased TIMI flow with Braunwald classes III, C and c as well as the angiographic correlates of the combined Braunwald classes.

Baseline characteristics of all patients were described, and the groups of patients with and without an identified culprit lesion were compared with one-way analysis of variance for continuous variables and a two-tailed Fisher exact test for categoric variables. Continuous variables were expressed as a mean value ± SD. Statistical significance was defined at $p < 0.05$. The group of patients with identifiable culprit lesions was further analyzed to correlate the acuteness or severity, or both, of their clinical presentation with the presence of a complex or thrombotic culprit lesion. In our analysis, acute or severe clinical presentation was assessed by each of the Braunwald classes as categoric variables (class III vs. classes I and II combined; class C vs. classes A and B; class c vs. classes a and b). Such analysis was in accordance with our hypothesis, and from a statistical point of view led to a more even distribution of patients among groups. Univariate analysis was performed in the same way.

To evaluate the independent angiographic predictors of the most acute or severe clinical presentations of UA, we conducted multivariate logistic regression analysis with the individual Braunwald classes (III, C and c) placed sequentially as the outcome. The model also controlled for all cardiac risk factors, history of previous percutaneous coronary intervention (in a nonculprit lesion) or previous coronary artery bypass graft surgery and multivessel disease. We further analyzed the combinations of the three highest Braunwald classes (IIIC, Cc and IIICc) in the same statistical model. The results were expressed as odds ratio and 95% confidence interval.

To investigate the ability of the Braunwald classification to predict complex lesions, total occlusions, intracoronary thrombus or decreased TIMI flow in the culprit artery, we performed an additional analysis in the same multivariate model: Each of the four angiographic variables was selected as the outcome, and classes III, C and c were sequentially evaluated as predictors of each angiographic finding. The statistical software JMP 3.1 for PowerPC (SAS Institute) was used.

Results

Descriptive statistics for all patients (n = 284) and patient groups with and without identified culprit lesions (n = 200 and n = 84, respectively) are shown in Table 1. As expected, patients in whom a single culprit lesion was not identified had a higher incidence of multivessel coronary artery disease (86%) and previous coronary artery bypass graft surgery (33%) than the other group (51% and 13%, respectively, $p < 0.05$). As mentioned previously, patients with a restenotic culprit lesion were excluded from our study. The overall incidence of class III UA was 54%, class C 17% and class c 37%. Classes A and a were significantly underrepresented in our study (1% and 11%, respectively). Furthermore, no patients with class A (secondary) UA had an identifiable culprit lesion.

Correlates of acute clinical presentation. Only the 200 patients with a single identifiable culprit lesion were included in the subsequent analyses. The overall incidence of complex

Table 1. Baseline Clinical Characteristics of Study Patients With or Without an Identifiable Culprit Lesion

	Total Patients (n = 284)	Culprit Lesion (n = 200)	No Culprit Lesion (n = 84)
Age (yr)	64 ± 11	62 ± 12	66 ± 10
Male	187 (66)	132 (66)	55 (65)
Smoking	69 (24)	51 (26)	18 (21)
Family hx of CAD	66 (23)	46 (23)	20 (24)
High cholesterol	121 (43)	87 (44)	34 (40)
Diabetes mellitus	78 (27)	49 (25)	29 (34)
Hypertension	187 (66)	133 (67)	54 (64)
Previous MI	107 (38)	72 (36)	35 (41)
Previous PTCA	74 (26)	56 (28)	18 (21)
Previous CABG	54 (19)	26 (13)	28 (33)*
Braunwald class			
I	76 (27)	57 (29)	19 (23)
II	56 (20)	34 (17)	22 (26)
III	152 (54)	109 (55)	43 (51)
A	1 (1)	0	1 (1)
B	234 (82)	158 (79)	76 (90)
C	49 (17)	42 (21)	7 (8)*
a	30 (11)	21 (11)	9 (10)
b	150 (53)	100 (50)	50 (60)
c	104 (37)	79 (39)	25 (30)
Multivessel disease	173 (61)	101 (51)	72 (86)*

*$p \leq 0.02$ between groups with and without an identifiable culprit lesion. Continuous variables expressed as mean value ± SD and categoric variables as number (%) of patients. CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; hx = history; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Table 2. Incidence of Angiographic Findings in Patients With an Identifiable Single Culprit Lesion

	Patients (n = 200)
Complex lesions	98 (49)
Intracoronary thrombus	28 (14)
Total occlusions	29 (14.5)
TIMI flow grade <3	61 (30.5)

Data are expressed as number (%) of patients. TIMI = Thrombolysis in Myocardial Infarction.

lesions in these patients was 49%, ICT 14%, total occlusions 14.5% and decreased TIMI flow 30.5% (Table 2).

Recent rest angina (Braunwald class III) was associated with a complex lesion in 56% of patients compared with 40% in classes I and II ($p = 0.04$ by univariate analysis). Intracoronary thrombus was detected in 18% of class III patients versus 9% in classes I and II ($p = 0.07$), and total occlusions occurred 19% in class III compared with 9% in classes I and II ($p = 0.04$ by univariate analysis only) (Table 3). The statistical significance of complex lesions was maintained in the multivariate model when we controlled for ICT but was eliminated by controlling for total occlusions and decreased TIMI flow. This was due to the very strong independent association of decreased TIMI flow with class III angina in 39% of patients (odds ratio 2.1, 95% confidence interval 1 to 4.2, $p = 0.003$ by multivariate analysis) and the association of a complex lesion with TIMI flow grade <3 ($p < 0.00001$).

Postinfarction angina (class C) was strongly associated with ICT (29% vs. 10% in class B) and decreased TIMI flow (48% vs. 26% in class B). These results remained significant after multivariate analysis as well (Table 4). Complex lesions were found in 60% of patients in class C versus 46% of those in class B ($p = 0.16$).

Intracoronary thrombus was detected in 21% of patients with UA refractory to maximal medical therapy (class c) compared with 9% in patients who responded to medical therapy ($p = 0.02$) (Table 5). Total occlusions, decreased TIMI flow and general definition of complex lesions were not directly associated with this clinical presentation. However, the incidence of all four angiographic characteristics was higher in class III than in classes I and II; class C than class B; and class c than classes a and b, even when 95% statistical significance was not achieved.

Subsequently, we combined the three highest Braunwald classes into the classes IIIC, IIIc, IIICc and Cc. Class IIIc had no patients. The other three classes were uniformly associated with ICT and TIMI flow grade <3 in our multivariate model (Table 6). Again, the incidence of complex lesions and total occlusions was also higher in those classes but did not achieve statistical significance by multivariate analysis.

Localization of the culprit artery correlated neither with clinical presentation, nor incidence of complex lesions or ICT, or both. The QCA analysis revealed no significant difference in minimal lumen diameter between the different Braunwald classes. The minimal lumen diameter was 0.8 ± 0.3 mm in patients in class III compared with 0.8 ± 0.4 mm in those in classes I and II ($p = 0.7$). The differences in percent area stenosis were also insignificant: 92.4 ± 0.2% in class III versus 91.6 ± 6.8% in classes I and II ($p = 0.5$). Similar QCA results were reproduced when class C was compared with class B and class c with classes a and b.

The separate analysis that aimed to evaluate the Braunwald classes as independent predictors of angiographic morphology yielded equally significant results to the previous analyses (Table 7). Class III angina was an independent predictor of complex lesions, total occlusions and TIMI flow grade <3. Class C predicted ICT, total occlusions ($p = 0.03$) and TIMI flow grade <3, whereas class c was predictive of ICT. Recent rest angina appeared to increase by two to three times the likelihood of decreased TIMI flow ($p = 0.007$), a complex lesion ($p = 0.02$) or a total occlusion ($p = 0.03$). Postinfarction angina quadrupled the chance of ICT ($p = 0.004$), and tripled the likelihood of decreased TIMI flow ($p = 0.004$), whereas refractory angina tripled the likelihood of ICT ($p = 0.01$).

Table 3. Correlation of Recent Rest Angina (Braunwald class III) With Angiographic Variables: Multivariate Analysis

	Class III (n = 109)	Classes I and II (n = 91)	OR (95% CI)	p Value
Complex lesions*	61 (56)	37 (41)	2.0 (1.1–3.8)	0.04
Intracoronary thrombus*	20 (18)	8 (9)	2.0 (0.8–5.3)	0.16
Total occlusions	21 (19)	8 (9)	1.0 (0.3–3.8)	ns
TIMI flow grade <3	43 (39)	18 (20)	2.0 (1.1–4.2)	0.03

*Before controlling for total occlusions and decreased Thrombolysis in Myocardial Infarction (TIMI) flow. Results are number (%) of patients. CI = confidence interval; OR = odds ratio.

Table 4. Correlation of Postinfarction Angina (Braunwald class C) With Angiographic Variables: Multivariate Analysis

	Class C (n = 42)	Class B (n = 158)	OR (95% CI)	p Value
Complex lesions	25 (60)	73 (46)	1.5 (0.5–4.3)	0.04
Intracoronary thrombus	12 (29)	16 (10)	5.6 (1.7–18.8)	0.005
Total occlusions	10 (24)	19 (12)	1.9 (0.4–8.9)	0.4
TIMI flow grade <3	20 (48)	41 (26)	3.6 (1.1–11.5)	0.03

Results are number (%) of patients. Abbreviations as in Table 3.

Table 5. Correlation of Refractory Unstable Angina (Braunwald class c) With Angiographic Variables: Multivariate Analysis

	Class c (n = 79)	Classes a and b (n = 121)	OR (95% CI)	p Value
Complex lesions	44 (56)	54 (45)	1.4 (0.7–2.7)	0.3
Intracoronary thrombus	17 (21)	11 (9)	2.9 (1.2–7.1)	0.02
Total occlusions	14 (18)	15 (12)	0.9 (0.2–3.1)	0.8
TIMI flow grade <3	28 (35)	33 (27)	0.8 (0.3–1.9)	0.6

Results are number (%) of patients. Abbreviations as in Table 3.

Table 6. Correlation of Combination of Braunwald Classes With Angiographic Variables: Multivariate Analysis

Braunwald Class	Incidence [n (%)]	ICT [OR (95% CI)]	TIMI Flow Grade <3 [OR (95% CI)]
Class IIIC	38 (19)	3.4 (1.2–9.3)	3.1 (1.2–8.4)
Class Cc	31 (16)	6.0 (1.9–19.3)	3.9 (1.3–11.6)
Class IIICc	28 (14)	6.4 (1.9–22.2)	4.1 (1.3–12.9)

ICT = intracoronary thrombus; other abbreviations as in Table 3.

Discussion

Most current data indicate that mural thrombus formation on an eroded, fissured or disrupted atherosclerotic plaque is the predominant pathophysiologic mechanism of UA (1,2). Although complex lesions or ICT, or both, have been collectively associated with UA both angiographically and angioscopically (21), their angiographic definitions are not standardized (7–10). The definitions of complex plaque and ICT overlap when the culprit artery is patent. We incorporated complex morphology, intracoronary thrombus and total occlusions into the general angiographic definition of complex lesions because they all contain some thrombus (7,18). Localized thrombus in lesions without filling defects may be platelet rich, whereas ICT may represent fibrin-rich thrombus (22). We prefer the term complex lesions rather than thrombotic lesions to collectively describe these angiographic findings because the former is similar to the pathologic term for a complicated plaque with superimposed thrombus (23,24).

Simple culprit lesions also occur in UA, but complex or thrombotic lesions have been associated with a worse prognosis (25). An increased incidence of MI, urgent revascularization or death in patients with complex versus simple lesions has been described in several studies (26–28). In contrast, clinical symptomatology (recurrent pain in the hospital) has high sensitivity but decreased sensitivity for an unfavorable outcome. Postinfarction angina (Braunwald class C) was associated with a worse prognosis both at 6 weeks and at 1-year follow-up comparison with primary UA (Braunwald class B) in a recent preliminary report (29).

Angioscopy is more sensitive than angiography for detection of ICT because it detects smaller thrombi not seen angiographically (30–33). However, angiography is relatively specific for ICT detection comparison with angioscopy (22,34). Therefore, the clinical correlates of such angiographic findings in UA have been appropriately sought in the most severe and acute clinical presentations. Similar correlation between lower levels of thrombosis and milder clinical cases should be attempted angioscopically.

The Braunwald classification provided the appropriate clinical tool for this type of analysis. The complexity of the classification underlines the clinical heterogeneity of UA. Previous studies have tested the angiographic and prognostic correlates of the Braunwald classification. In a retrospective analysis by Ahmed et al. (17), a high angiographic score, derived from a combination of variables, such as ICT, complex lesions and total occlusions, was associated with a high clinical score, which was derived from the combination of the various Braunwald classes. However, there was no direct correlation of any individual UA class with features of coronary morphology. The Braunwald classification was only recently shown to have prognostic implications (15,16,27).

In the present study, we used the highest levels of the Braunwald classification as markers of acute or severe clinical presentations and hypothesized that their presence correlated with the incidence of a complex lesion or ICT, or both. Absence of such angiographic characteristics may imply a lower degree rather than the absence of intracoronary thrombosis. Our results appear to support the initial hypothesis.

A consistent association was demonstrated between the most acute or severe clinical presentation as described by the individual higher rates of the Braunwald classification (III, C, c) and the angiographic findings of complex and thrombotic lesions, even if statistical significance was not reached in some instances. The lack of statistical significance in some cases was most likely due to an insufficient number of patients in certain clinical classes. However, the convergence of all the data supports the internal consistency of the results. Decreased TIMI flow also proved to be an important correlate of an acute clinical presentation (classes III and C), and the presence of a totally occluded vessel as well as any decrease in TIMI flow appeared to be responsible for the significant association of complex lesions and recent rest angina.

The presence of ICT rather than the more broad definition of complex lesions, was more strongly associated with higher Braunwald classes. We suspect that, as alluded to previously, angiographic ICT represents a higher thrombotic load than complex morphology without ICT, with the filling defects representing the presence of a fibrin-rich thrombus overlying a platelet-rich thrombus. Fibrin-rich thrombi may denote a greater degree of plaque disruption, increased hypercoagula-

Table 7. Validation of Individual Braunwald Classes as Independent Predictors of Angiographic Morphology: Multivariate Analysis

Braunwald Class	Complex Lesions [OR (95% CI)]	ICT [OR (95% CI)]	Total Occlusions [OR (95% CI)]	TIMI Flow Grade <3 [OR (95% CI)]
Class III	2.1 (1.1–3.9)*	2.3 (0.96–6.1)*	2.7 (1.1–7.3)*	2.6 (1.3–5.1)*
Class C	1.7 (0.8–3.7)	4.1 (1.6–10.6)	3 (1.1–8.1)*	3.1 (1.4–6.8)*
Class c	1.6 (0.8–2.9)	3.1 (1.3–7.4)*	1.6 (0.7–3.8)	1.4 (0.8–2.7)

*$p < 0.05$. Abbreviations as in Tables 3 and 6.

bility of the blood or more vasoconstriction with stasis of blood than complex morphology without ICT (35). This theory is supported by the strong association of ICT with post-MI angina. Acute MI is associated with the presence of fibrin-rich, red thrombi. Red thrombi have been detected angioscopically more commonly in patients with post-MI angina than in asymptomatic post-MI patients (28).

Furthermore, our results validate the highest levels of the Braunwald classification as powerful independent predictors of complex and thrombotic lesions. It is conceivable that one might use the Braunwald classification of UA to triage patients at the highest levels to more aggressive antithrombotic and early interventional treatment.

Study limitations. Angiography is specific but insensitive for the detection of ICT. We attempted to minimize this methodologic limitation by restricting the study to those UA cases that should be associated, because of their acute or severe presentation, with larger, angiographically detectable ICT. However, the incidence of thrombus would most likely have been increased had angioscopy been routinely performed.

The time to angiography was not standardized but was left to the decision of the primary cardiologist. However, assignment of Braunwald class was done at the time of angiography rather than on admission. Furthermore, not all patients with UA underwent catheterization. We enrolled only those patients who were referred for angiography. In our hospital, ~90% of all patients with UA are routinely referred for angiography, with the remaining 10% triaged to exercise testing or medical therapy, or both. It is likely that these more benign cases have a low incidence of angiographically detectable ICT (25). Therefore, their exclusion would probably not alter our results. Finally, the incidence of complex lesions was lower than reported in other angiographic studies, including our own work (8,11). Because 56% of patients received intravenous heparin before angiography, this may have decreased the incidence of complex lesions compared with that in other studies.

Conclusions. In this study, complex lesions and, specifically, ICT in addition to reduced coronary flow independently correlated with the clinical severity of the UA syndrome according to the Braunwald classification. In patients with postinfarction and refractory UA, this clinical presentation correlated with ICT and decreased TIMI flow. Recent rest angina also correlated with decreased TIMI flow and complex lesions, incorporating a high percentage of ICT and total occlusions. Additionally, the highest levels of the Braunwald classification were shown to be powerful independent predictors of complex and thrombotic lesion morphology.

These findings expand on previous data correlating angiography and clinical presentation in UA. They support the importance of thrombus formation on a presumed fissured or disrupted plaque as the most important pathophysiologic mechanism of the most acute or severe presentations of UA. Future studies may show that such patients presenting with the higher levels of the Braunwald UA classes derive increased benefit from newer antithrombotic or antiplatelet agents, such as the direct antithrombins or the IIb/IIIa inhibitors.

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